

### REMARKS

Claims 6-8 and 11-15 are pending. Claims 7, 12, 14 and 15 are withdrawn from consideration. Claims 6 and 11 are amended. Applicants reserve the right to file divisional/continuation applications to the cancelled subject matter. No new matter has been added.

Applicants submit that an unexecuted Declaration of Robert Market under 37 CFR 1.132 is provided with this response. An executed Declaration will be provided under separate cover.

### REJECTIONS UNDER 35 U.S.C. §102(b)

Claims 6 and 8 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by International Publication No. WO 98/13366. The Office Action alleges that disclosure of N-(3,4-dimethyl-5-isoxazolyl)-3-(phenylaminocarbonyl)thiophene-2-sulfonamide anticipates claims 6 and 8.

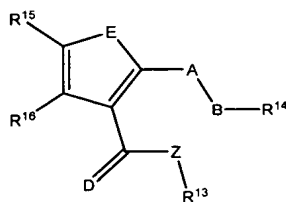
Applicants respectfully submit that N-(3,4-dimethyl-5-isoxazolyl)-3-(phenylaminocarbonyl)thiophene-2-sulfonamide disclosed in International Publication No. WO 98/13366 is not within the scope of instant claims because claim 6, as amended herein, requires R<sup>14</sup> to be phenyl and R<sup>13</sup> to be phenyl substituted with lower alkyl and heterocyclyl. Therefore, the reference does not anticipate claim 6 and claims dependent thereon. Applicants request reconsideration and removal of the rejection.

### REJECTIONS UNDER 35 U.S.C. §103(a)

#### 1. J. Med. Chem. 1999, 42, 4485-99

Claims 6, 8-11 and 13 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Wu *et al.*, *J. Med. Chem.* 1999, 42, 4485-99. The Office Action alleges that the difference between claimed subject matter and the cited reference is in scope and form. It is alleged that the reference teaches compounds that are positional isomers of the claimed compounds.

Applicants respectfully request reconsideration of the rejection in view of the amendments and remarks herein. As amended herein claim 6 is directed to compounds of Formula II:



(II)

where R<sup>13</sup> and R<sup>14</sup> are phenyl; R<sup>13</sup> is substituted with lower alkyl and heterocyclyl, and the remaining substituents are as defined therein.

**Teachings of Wu *et al.***

Wu *et al.* teaches 3-isoxazolylsulfamoyl-2-thiophenecarboxamide compounds as endothelin antagonists. All of the compounds described in Wu *et al.* possess an isoxazolylsulfamoyl group substituent at 3-position on the thienyl ring. Applicants respectfully submit that the compounds taught in the reference are structurally different than the compounds of formula II as claimed herein because the instant compounds possess a substituted phenylcarboxamide group at the 3-position on the thienyl ring. Examiner has the burden of establishing a *prima facie* case of obviousness by proving three elements: (1) a particular reference (or combined references) must suggest or teach all the limitations of the challenged claim, (2) a suggestion or motivation from the prior art to modify or combine the reference teachings, and (3) a reasonable expectation of success must exist from the prior art. MPEP §§2142, 2143, citing *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

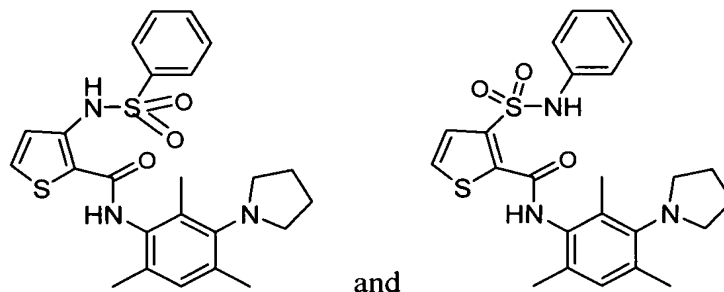
Applicants respectfully submit that the compounds of the instant claims do not overlap with the compounds taught in the cited reference. In particular, Wu *et al.* does not teach or suggest the substitution pattern on the thienyl ring as claimed herein. Thus, the reference fails to teach or suggest all of the claim limitations. Furthermore, Applicants respectfully submit that there is no suggestion or motivation from the prior art to modify the teachings of Wu *et al.* to replace, for example, the isoxazole group with a phenyl group. Additionally, even if only for the sake of argument such modifications were to be made, Applicants respectfully submit that Wu *et al.* does not and cannot indicate any reasonable expectation of success to one of ordinary skill in the art in connection with the claimed compounds in claim 6 and the claims dependent therefrom.

Accordingly, independent claim 6, and the claims dependent therefrom, are not obvious over the teachings of Wu *et al.* for at least these reasons. Applicants request

reconsideration and withdrawal of the rejection.

**Claim 11 and 13**

Applicants submit that claim 11 is directed to specific compounds:



Claim 13 depends from claim 11 and is directed to a pharmaceutical composition containing a compound of claim 11.

As discussed above, Wu *et al.* teaches 3-isoxazolylsulfamoyl-2-thiophenecarboxamide compounds as endothelin antagonists. The reference does not teach or suggest the phenylsulfamoyl substituent at 3-position on the thienyl ring. Applicants respectfully submit that Wu *et al.* does not teach or suggest all of the limitations of the claimed compounds. Furthermore, there is no suggestion or motivation from the prior art to modify the teachings of Wu *et al.* to arrive at the compounds of claim 11. Additionally, even if only for the sake of argument such modifications were to be made, Applicants respectfully submit that Wu *et al.* does not and cannot indicate any reasonable expectation of success to one of ordinary skill in the art in connection with the claimed compounds in claim 11 and the claims dependent therefrom.

Accordingly, claims 11 and 13 are not obvious over the teachings of Wu *et al.* Applicants request reconsideration and withdrawal of the rejection.

**2. WO 98/13366**

Claims 6, 8-11 and 13 are rejected under 35 U.S.C. § 103(b) as allegedly being obvious over WO 98/13366. Applicants requests reconsideration and removal of the rejection in view of the amendments and remarks herein.

**Claims 6 and 8**

Applicants submit that WO 98/13366 teaches a generic class of thiophene sulfonamides that have activity as endothelin antagonists. The reference discloses only one compound that possesses a 3-carboxamide group on a thiophene ring: N-(3,4-dimethyl-5-isoxazolyl)-3-(phenylaminocarbonyl)thiophene-2-sulfonamide. This compound possesses

an isoxazolylsulfamoyl group at 2-position and a phenylaminocarbonyl group at 3-position on the thiophene ring. As discussed above, claim 6 requires a phenylsulfamoyl group at 2-position and a phenylcarboxamide substituted with a lower alkyl and a heterocyclyl at 3-position on the thiophene.

Applicants respectfully submit that WO 98/13366 neither teaches or suggests the phenylsulfamoyl substituent at 2-position on the thienyl ring, nor does it teach or suggest the lower alkyl and heterocyclyl substituent on the phenylcarboxamide group as claimed herein. Thus, the reference fails to teach or suggest all of the claim limitations. Furthermore, Applicants respectfully submit that there is no suggestion or motivation from the prior art to modify the teachings of WO 98/13344 to replace, for example, the isoxazole group with a phenyl group and to arrive at the substitution pattern on the phenylcarboxamide group. In order for an obviousness rejection to be maintained, there must be some motivation in the prior art for one of ordinary skill in the art to modify the prior-art teaching so as to arrive at the claimed subject matter, with a reasonable expectation of success. In this case, there must be a suggestion to modify the compounds disclosed in WO 98/13366 such that they possess activity that is not specifically taught or suggested by the reference. Further, this alleged suggestion must be coupled with the expectation of successfully arriving at the compounds claimed herein. There is neither the suggestion nor the reasonable expectation of success in WO 98/13366.

Notwithstanding the failure of the reference to teach or suggest this particular class of thiophene sulfonamides, the compounds of claim 6 possess properties not taught or suggested by the reference. As described in the accompanying Declaration of Dr. Robert V. Market, the compounds are CCR9 antagonists. The Declaration provides data for exemplary compounds within the scope of the instant claims. Based on the teachings of the reference, one of skill in the art would not have predicted that the compounds within the scope of the instant claims would have activity as CCR9 antagonists.

Accordingly, independent claim 6, and the claims dependent therefrom, are not obvious over the teachings of WO98/13366. Applicants request reconsideration and withdrawal of the rejection.

#### **Claim 11 and 13**

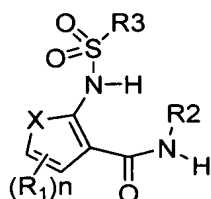
As discussed above, claim 11 is directed to specific compounds. The application describes that the compounds have activity as urotensin and CCR9 antagonists. Applicants

respectfully submit that WO 98/13366 does not teach or suggest the claimed compounds. Furthermore, there is no suggestion or motivation from the prior art to modify the teachings of WO 98/13366 to arrive at the compounds of claim 11. Additionally, even if only for the sake of argument such modifications were to be made, Applicants respectfully submit that WO 98/13366 does not and cannot indicate any reasonable expectation of success to one of ordinary skill in the art in connection with the claimed compounds in claim 11 and the claims dependent therefrom. Accordingly, claims 11 and 13 are not obvious over the teachings of WO 98/13366. Applicants request reconsideration and withdrawal of the rejection.

**3. WO 02/28353**

Claims 6, 8, 9 and 10 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over WO 02/28353. Applicants requests reconsideration and removal of the rejection in view of the amendments and remarks herein.

The Office Action alleges that the reference teaches compounds of formula II below for treatment of chronic renal failure and uremic bone disease:



Formula II

where X is sulfur or oxygen;

R<sub>1</sub> is independently selected from a group consisting of hydrogen, alkyl, aryl, haloalkyl, alkenyl, arylalkyl, arylalkenyl, halo, carboxy, carboalkoxy, carbamyl, alkyl oralkylcarbamyl, cyano, alkoxy, hydroxyl, amino or alkylamino, nitro, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, sulfamyl, aryl or alkylsulfonamido, or represents a fused ring forming a benzothiophene, or(R<sub>1</sub>)<sub>n</sub> represents a(R<sub>1</sub>)<sub>n</sub> substituted aryl or a heterocycle selected from the group consisting of thiophene, furan, pyridine, pyrimidine, pyrazine, isoxazole, thiazole, imidazole, pyrazole, thiadiazole, oxadiazole, and benzo analogs thereof; or R<sub>1</sub> represents a fused ring selected from the group consisting of thiophene, furan, pyridine, pyrimidine, pyrazine, isoxazole, thiazole, imidazole, pyrrazole, thiadiazole, oxadiazole, and benzo analogs thereof, and

R<sub>2</sub> and R<sub>3</sub> are not hydrogen, but are independently selected from a group consisting of- (CHR<sub>4</sub>)<sub>n</sub>-(CHR<sub>5</sub>)<sub>m</sub>-(CHR<sub>6</sub>)<sub>p</sub>-(R<sub>1</sub> substituted aryl or heteroaryl), alkyl, haloalkyl, or alkyl

interrupted by one or more oxygen or sulfur atoms. The carbon chain may also contain a double bond. m, n, and p are independently 0-3.

As discussed above, instant claim 6 requires a phenylsulfamoyl at 2-position and a phenylcarboxamide substituted with a lower alkyl and a heterocyclyl at 3-position on the thiophene. Applicants respectfully submit that such compounds are not taught or suggested in the reference. The reference discloses only one compound that possesses a 3-carboxamide group on a thiophene ring: 2-benzenesulfonylamino-thiophene-3-carboxylic acid 4-chlorophenylamide. This compound is monosubstituted at the carboxamide phenyl group. As discussed above, the instant claim requires a lower alkyl and a heterocyclyl group substituent at that position. The reference does teach or suggest this substitution pattern.

Notwithstanding the failure of the reference to teach or suggest this particular class of thiophene sulfonamides, the compounds of claim 6 possess properties not taught or suggested by the reference. As described in the accompanying Declaration of Dr. Robert V. Market, the compounds possess activity as CCR9 antagonists. The Declaration provides data for exemplary compounds within the scope of the instant claims. Based on the teachings of the reference, one of skill in the art would not have predicted that the compounds within the scope of the instant claims would have activity as CCR9 antagonists.

The reference does not provide any suggestion to modify the compounds disclosed in WO 02/28353 such that they possess activity that is not specifically taught or suggested by the reference. Further, this alleged suggestion must be coupled with the expectation of successfully arriving at the compounds claimed herein. There is neither the suggestion nor the reasonable expectation of success in WO 02/28353.

Accordingly, independent claim 6, and the claims dependent therefrom, are not obvious over the teachings of WO 02/28353. Applicants request reconsideration and withdrawal of the rejection.

#### **Claim 11 and 13**

As discussed above, claim 11 is directed to specific compounds. The application describes that the compounds have activity as urotensin and CCR9 antagonists. Applicants respectfully submit that WO 02/28353 does not teach or suggest the claimed compounds. Furthermore, there is no suggestion or motivation from the prior art to modify the teachings of WO 02/28353 to arrive at the compounds of claim 11. Additionally, even if only for the sake of argument such modifications were to be made, Applicants respectfully submit that

WO 02/28353 does not and cannot indicate any reasonable expectation of success to one of ordinary skill in the art in connection with the claimed compounds in claim 11 and the claims dependent therefrom. Accordingly, claims 11 and 13 are not obvious over the teachings of WO 02/28353. Applicants request reconsideration and withdrawal of the rejection.

**DOUBLE PATENTING**

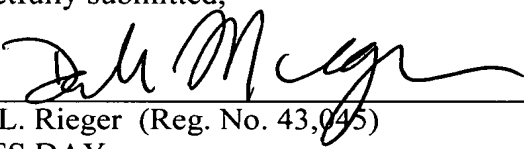
Claims 11 and 13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over copending Application No. 10/924,180. Applicants hereby request that the rejection be held in abeyance until an indication of patentable subject matter is given, at which point a need for Terminal Disclaimer may be evaluated.

\*\*\*\*\*

In view of the above, allowance of the application is respectfully requested. Please apply any charges or any credits to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

Date: June 13, 2007

  
\_\_\_\_\_  
Dale L. Rieger (Reg. No. 43,045)  
JONES DAY  
222 East 41st Street  
New York, New York 10017  
(858) 314-1200